REMARKS

Claims 48-62 and 92-93 are pending in the subject application. By this Amendment, applicants have amended claims 48, 49, 54, 57, 90 and 93.

The amendments to claim 48 are supported in the specification at, *inter alia*, page 19, lines 30-32 and page 25, line 29 to page 26, line 11. The amendments to claims 57, 60 and 93 are supported in the specification at, *inter alia*, page 19, lines 30-32. Thus, these amendments do not raise any issue of new matter. Similarly, no new matter is introduced by the amendment to claim 49 which merely involves a formatting change. The amendment to claim 54 corrects an obvious typographical error and also does not raise any issue of new matter. Applicants note that the same typographical error has also been corrected by an amendment to the paragraph on page 22, lines 9-19. Since the above-identified amendments do not raise any issue of new matter, applicants respectfully request that the Examiner enter this Amendment. Upon entry of this Amendment, claims 48-62 and 92-93 will still be pending and under examination.

The Claimed Invention

This invention provides an isolated antibody which binds to an isolated polypeptide comprising consecutive amino acids having the sequence set forth in SEQ ID NO:2, or a fragment thereof, encoded by a nucleic acid which encodes a Kaposi's sarcoma-associated herpesvirus (KSHV; also called human herpesvirus 8, HHV8) latency-associated nuclear antigen 2 (LANA2) polypeptide or a fragment thereof. The invention also provides related compositions and diagnostic and therapeutic methods. The existence of a LANA2 polypeptide in KSHV was not known prior to the disclosures in the subject specification.

Priority Claim

The Examiner stated that an application which claims the benefit of an earlier application must contain a specific reference to the prior application in the first sentence of the specification or in an application data sheet (citing 37 C.F.R. §1.78(a)(2) and (a)(5)). The Examiner also stated that the specific reference to any nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. The Examiner requested that applicants update the priority information by including the patent number.

In response, applicants have hereinabove amended the specification to provide the U.S. Patent No. and issue date of the parent application to which the present application claims priority.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 48-62 and 92-93 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner stated that claim 48 is vague and indefinite since the intended metes and bounds of the polypeptide are not defined. The Examiner also stated that, moreover, the intended metes and bounds of the antibody are not defined. The Examiner further stated that, in addition, the claim is confusing for recitation of "capable" of binding, since this limitation does not set forth positively whether or not the intended antibody actually does "specifically" bind to the protein. The Examiner also stated that, in addition, the claim is confusing for

recitation of the term "specifically." The Examiner stated that this is a relative term, subject to varied interpretation. The Examiner further stated that the claim has been interpreted in light of the specification and since there is no teaching of specificity or capability, or even of an antibody, the claim is considered to be vague and indefinite. The Examiner also stated that this rejection applies to the dependent claims.

In response, applicants respectfully traverse this rejection.

Applicants note, without conceding the correctness of the Examiner's position, that claim 48, as amended, specifies that the subject polypeptide comprises consecutive amino acids having the sequence set forth in SEQ ID NO:2. Applicants therefore maintain that the metes and bounds of the polypeptide are clearly defined in claim 48, as amended. Applicants also note that claim 48, as amended, does not recite the terms "capable of binding" or "specifically." Applicants therefore request that the Examiner withdraw this rejection of claim 48 and also claims 49-62, 92 and 93 which depend, directly or indirectly, from claim 48 and therefore necessarily recite all its limitations.

The Examiner stated that claim 57 is vague and indefinite because the intended metes and bounds of the polypeptide are not defined. The Examiner also stated that this rejection applies to the dependent claims.

In response, applicants respectfully traverse this rejection.

Without conceding the correctness of the Examiner's position, applicants note that claim 57, as amended, specifies that the subject polypeptide comprises consecutive amino acids having the sequence set forth in SEQ ID NO:2. Thus, applicants maintain that the metes and bounds of the polypeptide are clearly defined in claim 57, as amended, and in dependent claims 58, 59, 61 and

62 which necessarily recite all the limitations of claim 57.

The Examiner stated that claim 92 is vague and indefinite because the intended metes and bounds of the antibody are not defined. The Examiner requested clarification as to whether applicants' intent is to claim a patient's serum antibody. The Examiner also stated that this rejection applies to the dependent claims.

In response, applicants respectfully traverse.

Applicants note that claim 92 depends from claim 48. As discussed above, applicants maintain that claim 48, as amended, is not vague and indefinite. In particular, applicants note that claim 48, as amended, is directed to an *isolated* antibody and, thus, is not directed to patient serum antibody. Applicants therefore maintain that the metes and bounds of the antibody are clearly defined in claim 92 and hence also in dependent claim 93.

Rejections under 35 U.S.C. §101

The Examiner rejected claims 48-62 and 92-93 are rejected under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter.

The Examiner stated that claims 48-62 and 92-93, as written, do not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. The Examiner also stated that in the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter (citing *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980)). The Examiner stated that the claims should be amended to indicate the

hand of the inventor, e.g., by reciting an "isolated" or "purified" antibody as taught in the specification (citing M.P.E.P. §2105).

In response, applicants respectfully traverse.

Without conceding the correctness of the Examiner's position, applicants note that claim 48, as amended, is directed to an "isolated" antibody, consistent with the Examiner's recommendation. Applicants therefore respectfully submit that this rejection should be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph

Written Description

The Examiner rejected claims 48-62 and 92-93 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner stated that in the instant disclosure, applicants have only disclosed the protein sequence identified as SEQ ID NO:2 that is directed to LANA2. The Examiner also stated that the art of raising an antibody against a disclosed protein is routine, and hence, even though the specification has not taught a specific antibody or antibodies of any kind, it is concluded that an antibody against the protein sequence designated SEQ ID NO:2 finds sufficient written description in the original disclosure. The Examiner further stated that, however, no other protein sequences were disclosed, and as a consequence it would be impossible to raise an antibody against undisclosed sequences. The Examiner additionally stated that, in other words, raising or detecting antibodies against sequences that lack written description would

be rather impossible if the structure of the protein is not defined.

The Examiner stated that the specification does not set forth the metes and bounds of those protein sequences other than SEQ ID NO:2, and there is not enough information in the literature to guide one of ordinary skill in the art in predicting the undisclosed sequences. The Examiner also stated that, therefore, a written description of the other claimed sequences or antibodies that specifically bound the proteins should be disclosed to overcome this rejection (citing *University of California* v. *Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997).

In response, applicants respectfully traverse this "written description" rejection.

Without conceding the correctness of the Examiner's position, applicants note that claims 48, 57, 60 and 93, as amended, specify that the polypeptide recited in these claims comprises consecutive amino acids having the sequence set forth in SEQ ID NO:2. Applicants note the Examiner's explicit statement that an antibody against the protein sequence designated SEQ ID NO:2 finds sufficient written description in the original disclosure. Applicants maintain, therefore, that the subject specification provides an adequate written description of the subject matter of claims 48, 57, 60 and 93, as amended, and the claims which depend therefrom.

Enablement

The Examiner rejected claims 48-62 and 92-93 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for forming antibodies against SEQ ID NO:2, allegedly does not reasonably provide enablement for raising antibodies against any and all LANA2 polypeptides of HHV-8. The Examiner

stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The Examiner reminded applicants that the state of the art in this field is considered to be highly unpredictable, even though the skill in this art is considered to be high (referring applicants to *Fiers v. Revel* (25 USPQ2d 1601 at 1606) and *Genentech, Inc. v. Novo Nordisk A/S* (42 USPQ2d 1001-1007). The Examiner quoted the CAFC in *Genentech* that "[i]t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute enablement" (citing page 1005). The Examiner stated that applicants cannot rely on the knowledge of those skilled in the art to enable the claims without providing adequate teaching. The Examiner also stated that due to a lack of adequate teaching, undue experimentation would be required to enable the full scope of the claimed invention.

The Examiner stated that, at the onset, the Patent Office concedes that the art of raising an antibody against a known protein is routine. The Examiner also stated that, however, raising antibodies against an unknown protein is not routine, and if the structure of the protein is not provided it would be nearly impossible to form an antibody or detect any antibody or diagnose any diseases. The Examiner further stated that applicants have taught the SEQ ID NO:2 sequence, and even though no antibody has been taught, forming an antibody against SEQ ID NO:2 or detecting SEQ ID NO:2 is routine, but raising antibodies against an unknown protein is not routine. The Examiner additionally stated that the claimed antibodies are formed against a specific peptide, i.e., SEQ ID NO:2 but that there is no teaching about any other polypeptide. The Examiner also stated that absent adequate teaching, one of ordinary skill in the art would be forced into undue experimentation to enable the full scope of the claimed invention. The Examiner concluded

that, therefore, considering the large quantity of experimentation needed, the unpredictability of the field, the state of the art, and breadth of the claims (citing *In re Wands*, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988), undue experimentation would be required to enable the intended claim.

In response, applicants respectfully traverse this "enablement" rejection.

Without conceding the correctness of the Examiner's position, applicants note again that claims 48, 57, 60 and 93, as amended, specify that the polypeptide recited in these claims comprises consecutive amino acids having the sequence set forth in SEQ ID NO:2. Applicants note that the Examiner has conceded that generating an antibody against SEQ ID NO:2 or detecting SEQ ID NO:2 is routine. Applicants understand this to mean that generating an antibody against SEQ ID NO:2 or detecting SEQ ID NO:2 is enabled by the specification as filed. Thus, applicants maintain that the subject specification adequately enables claims 48, 57, 60 and 93, as amended, and the claims which depend therefrom. Accordingly, applicants request that the Examiner withdraw this "enablement" rejection under 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. §102(b)

The Examiner rejected claims 48-62 and 92-93 under 35 U.S.C. §102(b) as allegedly anticipated by Rainbow et al. (J. Virol. [1997] 71(8): 5915-5921). The Examiner stated that the broad limitation of the claimed invention is anticipated by this reference. According to the Examiner, Rainbow et al. teaches antibodies against LANA of HHV-8, and detected serum antibodies against Kaposi's sarcoma (citing the abstract, and page 5916, left column, third full paragraph, and page 5920, second paragraph). The Examiner stated that the product disclosed in

the above-cited art appears to be identical to, or so similar that it is indistinguishable from, the product claimed by applicants. The Examiner also reminded applicants that the Patent Office does not have facilities to perform physical comparisons between the claimed product and similar prior art products. The Examiner stated that, hence, the teaching of the above-cited art anticipates the claimed invention. The Examiner further stated that, moreover, if the prior art structure is capable of performing the intended use, then it meets the claim (citing *In re Casey,* 152 USPQ 235 [CCPA 1967] and *In re Otto,* 136 USPQ 458, 459 [CCPA 1963]).

In response, applicants respectfully traverse the rejection of claims 48-62 and 92-93 as anticipated by Rainbow et al.

Applicants respectfully point out to the Examiner that Rainbow et al. teaches antibodies to LANA1, not antibodies to LANA2 as claimed in the instant application. In support of this statement, applicants note that the LANA polypeptide (LANA1) taught by Rainbow et al. is encoded by orf73 (see the abstract and page 5916, first full paragraph; see also page 2, lines 17-19 of the subject specification which equates ORF73 with LANA1). By contrast, the LANA2 polypeptide taught in the subject application is an unrelated polypeptide encoded by orf10.5 (see the specification at, *inter alia*, page 53, line 32 to page 54, line 1). Indeed, the subject specification explicitly distinguishes between LANA1 and LANA2 (see, *inter alia*, page 5, lines 16-18; page 54, lines 20-33; page 58, lines 23-24; and page 59, lines 29-34), citing Rainbow et al. (1997) as a reference for LANA1 (see page 54, lines 23-24). The specification also teaches that the orf10.5 (K10.5) gene which encodes LANA2 had not been identified prior to applicants' disclosure of this gene (see the specification at, *inter alia*, page 4, lines 9-11). In this regard, applicants note that the orf10.5 transcript encoding LANA2 is generated by a novel splicing event that was not

predicted by sequence analysis of the KHSV genome prior to applicants' disclosures in the instant specification (see the specification at, *inter alia*, page 52, line 13 to page 53, line 30). Applicants therefore respectfully submit that the rejection of claims 48-62 and 92-93 as anticipated by Rainbow et al. is without merit.

The Examiner also rejected claims 48-50 under 35 U.S.C. §102(b) as allegedly anticipated by Chang et al. (WO 98/04576). The Examiner stated that the antibody taught in this reference (citing claims 14, 17, 18, 19) clearly anticipates the broad limitations of the claimed invention. The Examiner also stated that the product disclosed in the above-cited art appears to be identical to, or so similar that it is indistinguishable from, the product claimed by applicants. The Examiner further stated that the antibodies have long range of detestability, and absent side by side comparison, it is determined that the products are the same.

In response, applicants respectfully traverse the above rejection.

Applicants note that claim 17 of PCT International publication No. WO 98/04576 teaches antibodies to the following KHSV polypeptides as recited in claim 1: viral macrophage inflammatory protein II; viral interleukin 6; viral interferon regulatory factor 1; complement-binding protein; glycoprotein B; capsid protein IV encoded by orf65; immediate early protein encoded by orf73; glycoprotein M; and glycoprotein L. As noted above, the LANA2 polypeptide taught in the subject application is encoded by orf10.5 (see the specification at, *inter alia*, page 53, line 32 to page 54, line 1). Applicants assert that neither this polypeptide nor any antibody to it is taught in WO 98/04576. Applicants maintain, therefore, that the rejection of claims 48-50 as anticipated by Chang et al. should be withdrawn.

The Examiner rejected claims 48-62 and 92-93 under 35 U.S.C. §102(b) as allegedly anticipated by Zhu et al. (Virology [1999] 256: 381-392). The Examiner stated that Zhu et al. teaches antibodies against LANA of HHV-8 and detected serum antibodies against Kaposi's sarcoma (citing the abstract). The Examiner further stated that Zhu et al. also teaches antibody labeling (citing page 384, first full paragraph) and a method of determining disease (citing page 389, left column, first full paragraph). The Examiner also stated that the product disclosed in the above-cited art appears to be identical to, or so similar that it is indistinguishable from, the product claimed by applicants. The Examiner further stated that, hence, the teaching of the above-cited art anticipates the claimed invention.

In response, applicants respectfully traverse the above rejection.

Applicants respectfully point out to the Examiner that, like Rainbow et al. discussed above, Zhu et al. teaches antibodies to LANA1, not antibodies to LANA2 as claimed in the instant application. This is evident from Zhu et al.'s description of their latent antigen as ORF73 (see, e.g., the abstract and page 388, first paragraph of Discussion) which is identified as the same ORF73 used by Rainbow et al. (see page 388, second paragraph of Discussion). By contrast, as noted above, the LANA2 polypeptide taught in the subject application is an unrelated polypeptide encoded by orf10.5 (see the specification at, *inter alia*, page 53, line 32 to page 54, line 1). Accordingly, applicants maintain that the rejection of claims 48-62 and 92-93 as anticipated by Zhu et al. is unfounded.

The Examiner rejected claims 48-62 and 92-93 under 35 U.S.C. §102(b) as allegedly anticipated by Kellam et al. (J. Virol. [1999] 73(6): 5194-5155). The Examiner stated that the broad

limitation of the claimed invention is anticipated by this reference. The Examiner also stated that Kellam et al. teaches antibodies against LANA of HHV-8, and detected serum antibodies against Kaposi's sarcoma (citing the abstract). The Examiner further stated that Kellam et al. also teaches antibody labeling (citing Figure 1) and a method of determining disease (citing page 5152, right column, first full paragraph, and page 5154, last paragraph). The Examiner also stated that the product disclosed in the above-cited art appears to be identical to, or so similar that it is indistinguishable from, the product claimed by applicants.

In response, applicants respectfully traverse the rejection of claims 48-62 and 92-93 as anticipated by Kellam et al.

Applicants respectfully point out to the Examiner that Kellam et al. teaches antibodies to LANA1, not antibodies to LANA2 as claimed in the instant application. In this regard, applicants note that the LNA polypeptide (LANA1) taught by Kellam et al. is encoded by orf73 (see, e.g., the second sentence of the abstract) which generates a 5.2 kb transcript (see page 5149, second paragraph), and is expressed in KS nodules (see page 5149, right col., full paragraph). By contrast, the LANA2 polypeptide taught in the subject application is a different polypeptide which is encoded by orf10.5 (see the specification at, *inter alia*, page 53, line 32 to page 54, line 1), generates a 1704 bp transcript (see the specification at page 53, lines 23-26), and is not expressed in KS lesions (see the specification at page 5, lines 9-12). Applicants therefore respectfully submit that the rejection of claims 48-62 and 92-93 as anticipated by Kellam et al. should be withdrawn.

Rejections under 35 U.S.C. §102(a)

The Examiner rejected claims 48-62 and 92-93 under 35 U.S.C.

§102(a) as allegedly anticipated by Pierrotti et al. (J. Clin. Virol. [2000] 16: 247-251). The Examiner stated that the broad limitation of the claimed invention is anticipated by this reference. The Examiner also stated that Pierrotti et al. teaches antibodies against LANA of HHV-8, and detected serum antibodies against Kaposi's sarcoma (citing the abstract). The Examiner further stated that Pierrotti et al. also teaches antibody labeling (citing page 384, first full paragraph; *sic*) and a method of determining disease (citing page 389, left column, first full paragraph; *sic*). The Examiner additionally stated that the product disclosed in the above-cited art appears to be identical to, or so similar that it is indistinguishable from, the product claimed by applicants.

In response, applicants respectfully traverse the rejection of claims 48-62 and 92-93 as anticipated by Pierrotti et al.

Applicants note that although Pierrotti et al. does not provide details on the molecular or biochemical properties of the LANA antigen for which immunological screening was performed, it is evident that this polypeptide was LANA1. Thus, for example, Pierrotti et al. identify the antigen simply as "LANA" without any numeral designation. This is reflective of the fact that the research was conducted prior to the discovery by applicants of a second KSHV latency-associated nuclear antigen which necessitated the designation of distinct LANA1 and LANA2 antigens. Furthermore, Pierrotti et al.'s data were reported to be consistent with the data of Gao et al. (1996) and Lennette et al. (1996) on immunological detection of LANA (see page 248, third paragraph, and page 250, second paragraph), which in 1996 necessarily referred to LANA1. Since the subject application claims antibodies to the LANA2 polypeptide which are unrelated to Pierrotti et al.'s LANA1 antibodies, applicants maintain that the rejection of claims 48-62 and 92-93 as anticipated by Pierrotti et al. is without merit.

Rejections under 35 U.S.C. §102(e)

The Examiner rejected claims 48-50 under 35 U.S.C. §102(e) as allegedly anticipated by Haas et al. (U.S. Patent No. 6,319,667 B1). The Examiner stated that the antibody taught in this reference (citing the claims) clearly anticipates the broad limitations of the claimed invention. The Examiner also stated that the product disclosed in the above-cited patent appears to be identical to, or so similar that it is indistinguishable from, the product claimed by applicants.

In response, applicants respectfully traverse the rejection of claims 48-50 as anticipated by Haas et al.

Applicants note that the antibodies produced by Haas et al. were directed against a "kaposin" polypeptide which is encoded by the KSHV T0.7 transcript (see col. 3, lines 26-29; col. 4, lines 22-23; and Figure 2). Applicants note further that the kaposin polypeptide in unrelated to the LANA2 polypeptide disclosed in the subject specification. For example, Haas et al. disclose that kaposin contains three very short ORFs (see col. 1, lines 59-62) which exhibit no known homologies to other viral proteins (see col. 8, lines 17-18) and are thus not homologous to LANA2. Moreover, kaposin is expressed on the cell surface (see Haas et al., col. 8, line 13) whereas LANA2 is expressed in the nucleus (see specification at page 53, lines 32-34). In addition, LANA2 inhibits p53 activity (see specification at page 55, line 34 to page 56, line 24) whereas there is no indication that kaposin affects p53 activity, and it is unlikely that the cell surface-localized kaposin peptide would inhibit the activity of p53 which is a nuclear protein. Because LANA2 is completely unrelated to the kaposin peptide taught by Haas et al., applicants maintain that Haas et al.'s disclosure of antibodies to kaposin do not anticipate claims 48-50 of the present application.

Conclusion

In view of the remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the claim rejections set forth in the June 17, 2004 Office Action, and earnestly solicit allowance of all claims pending in the subject application.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invites the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450.

9/17/04
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